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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,644	01/15/2004	Peter Wernet	07588/026003	5815

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EXAMINER	
NGUYEN, QUANG	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/758,644	WERNET, PETER	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-9* is/are pending in the application.

4a) Of the above claim(s) *3 and 5-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/27/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 5/16/07 was entered.

Claims 1-3 and 5-9 are pending in the present application.

Claims 3 and 5-9 were withdrawn previously from further consideration because they were directed to non-elected inventions.

Accordingly, amended claims 1-2 are examined on the merits herein.

Response to Amendment

The rejection under 35 USC 102(b) as being anticipated by Naughton et al (US 5,842,477) as evidenced by Ha et al. (US 2005/0118714 A1) is withdrawn in light of Applicant's amendment.

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. ***This is a new ground of rejection necessitated by Applicant's amendment.***

Amended independent claim 1 recites the limitation "**whereby said USSCs regenerate cardiac muscle in said patient and treat said disease**". In the amendment filed on 5/16/07 (page 6), Applicants cited original claim 1; page 1, line 19 through page 2, line 2; page 2, lines 16-28; page 7, lines 22-29; and page 20, line 20 through page 21, line 21 as alleged supports for the above limitation. Apart from the disclosure that the unrestricted somatic stem cells (USSCs) of the present invention are capable to differentiate into mesenchymal stem or progenitor cells, hematopoietic lineage stem cell or progenitor cells, neural stem or progenitor cells or endothelial stem or liver progenitor cells, none of the cited passages and the original claim 1 teaches specifically that the unrestricted USSCs are capable of differentiating specifically into cardiomyocytes, and thereby regenerate cardiac muscle (made up of cardiomyocytes) in a human patient in need of treatment for cardiac muscle disease. Thus, there is **no written support** in the originally filed specification for the method of treating a cardiac muscle disease in a human patient in need of treatment for cardiac muscle disease by administering to said patient human USSCs, so that the USSCs regenerate cardiac muscle in said patient. Please note that cardiomyocytes are a specific type of muscle cells. They are structurally distinct from other muscle cells such as smooth muscle cells and skeletal muscle cells, and they possess different properties from those of these other muscle cells. The concept of the presently amended method is not supported by the present application, or by the specifications of the U.S. Serial No. 09/985,335, filed on 11/2/2001 and the provisional application 60/245,168, filed on 11/03/2000, to which the present application claims priority to. It is further noted that

original claim 4 of the present application is the only generic written support for a method of treating a disease of the cardiac muscle using human USSCs, without any indication that the administered USSCs are capable of regenerating cardiac muscle or cardiomyocytes in the treated patient.

Therefore, given the lack of sufficient guidance provided by the originally filed specification, it would appear that Applicants did not contemplate or had possession of the instantly claimed invention at the time this application was filed (1/15/04), let alone at the filing dates of 11/02/2001 and 11/3/2000.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Amended claims 1-2 are rejected under 35 U.S.C. 102(e) as being anticipated by Sandberg et al. (US 2004/0197310 A1 with an effective filing date of 2/12/2003) as evidenced by Ha et al. (US 2005/0118714 A1; Cited previously). ***This is a new ground of rejection necessitated by Applicant's amendment.***

Sandberg et al discloses at least a method for treating myocardial infarctions in an individual by administering an effective amount of a composition comprising an

human umbilical cord blood cell, including a human umbilical cord blood mesenchymal cell, to produce cardiac muscle cells in the heart of the individual, and wherein the umbilical cord blood cell differentiates into a cardiac muscle cell (see at least Summary of the Invention; particularly paragraphs 21-23; paragraphs 34, 43, 49; examples and claims). Sandberg et al further teaches that the umbilical cord blood composition comprises a mononuclear cell fraction isolated from human umbilical cord blood, containing mesenchymal stem or progenitor cells (paragraphs 49, 51, 53). Sandberg et al further discloses that human umbilical cord blood cells with a mesenchymal phenotype express SH2, SH3, SH5, alpha-smooth muscle actin, CD13, CD29 and CD49, and the immunotype and functional displayed by these cord blood-derived mesenchymal cells closely resembles the characteristics assigned to bone marrow derived mesenchymal progenitor cells (page 2, bottom of paragraph 15). Therefore, the human umbilical cord blood mesenchymal cell or a composition comprising the same taught by Sanberg et al. would possess cells with cellular markers positive for the CD13 and CD29 antigens, while negative for the CD14 and CD45 antigens and lack expression of hyaluronan synthase. To further support the examiner's position, Ha et al. teaches clearly that human umbilical cord-blood derived mesenchymal stem/progenitor cells have immunophenotypic characteristics in that they are positive for CD29, CD49e, CD44, CD54, CD13, CD90, SH2, SH3 and SH4 antigens and negative for CD45, CD34, CD14, HLA-DR, CD31, CD51/61, CD49d, CD`106 and CD64 antigens (paragraph 0027).

Accordingly, the teachings of Sandberg et al anticipate the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Pittenger et al. (WO 99/03973) in view of Erices et al. (British Journal of Haematology 109:235-242; IDS). ***This is a new ground of rejection necessitated by Applicant's amendment.***

Pittenger et al already discloses a method of administering to the heart of an individual a cardiomyocyte producing amount of human mesenchymal stem cells to regenerate or repair striated cardiac muscle that has been damaged through disease or degeneration, such as ischemic hearts and congestive heart failure patients (see at least Summary of the Invention, pages 2-4).

Pittenger et al does not teach specifically the use of human mesenchymal stem cells that are obtained from umbilical cord blood.

However, at least at the filing date of the present application Erices et al. already taught the preparation of a homogeneous population of adherent cells showing a fibroblastoid morphology (mesenchymal-like cells) by culturing mononuclear cells isolated from human umbilical cord blood in a medium containing fetal bovine serum (see Abstract, Materials and Methods, particularly Fig. 1B,D, F). The mesenchymal-like

cells express antigens **CD13, CD29, CD49e, CD54, CD90, but did not express antigens CD14, CD34, CD45, CD49d, CD106 or endothelial-related antigens CD31 and von Willebrand factor** (under the section tilted Characteristics of mesenchymal-like cells). Additionally, Erices et al. taught that under appropriate culture cell medium, the mesenchymal-like cells can differentiate into osteoblasts and adipocytes. Thus, these cord blood-derived mesenchymal cells display a function and an immunophenotype closely resembles the characteristics assigned to bone marrow derived mesenchymal progenitor cells. Erices et al also discloses that preterm, as compared with term, cord blood is richer in mesenchymal progenitors (see page 241, col. 2, second paragraph). Moreover, Erices et al teaches specifically that based on their large *ex vivo* expansion capacity as well as on their differential potential, cord blood-derived mesenchymal progenitor cells can be visualized as attractive targets for cellular or gene transfer therapeutic options (page 241, col. 2, third paragraph).

It would have been obvious for an ordinary skilled artisan to modify the teachings of Pittenger et al by also using the cord blood-derived mesenchymal cells that display a function and an immunophenotype closely resembles the characteristics assigned to bone marrow derived mesenchymal progenitor cells to regenerate or repair striated cardiac muscle that has been damaged through disease or degeneration in a patient in need thereof, in light of the teachings of Erices et al.

An ordinary skilled artisan would have been motivated to carry out the above modification because Erices et al also taught specifically that based on their large *ex vivo* expansion capacity as well as on their differential potential, cord blood-derived

mesenchymal progenitor cells can be visualized as attractive targets for cellular or gene transfer therapeutic options.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of Pittenger et al., Erices et al., coupled with a high level of skill of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

The examiner notes that identical teachings of Pittenger et al. (WO 99/03973) can also be found in US 6,387,369.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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QUANG NGUYEN, PH.D.
PRIMARY EXAMINER